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Evaluating the predictive performance of nutritional indices in postoperative outcomes following pancreaticoduodenectomy in the elderly

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ABSTRACT

Aims: The aim of the study was to evaluate the prognostic significance of nutritional indices including geriatric nutritional risk index (GNRI), prognostic nutritional index (PNI), and total bilirubin-albumin ratio (TBAR) in predicting postoperative outcomes following pancreaticoduodenectomy (PD) among elderly patients.

Methods: This study retrospectively analyzed 192 patients aged 65 and older who underwent PD at a single center. Postoperative complications were graded using the Clavien-Dindo classification. Postoperative survival was defined as survival beyond 90 days. All deaths that occurred during follow-up were included in the assessment of long-term mortality. In addition, the duration of hospital stay was assessed.

Results: The mean age of the participants was 71.6±5.3 (range: 65–87) years. The mean follow-up time was 22.5±20.9 months (median: 15.0 months, IQR: 6.0-36.0). Postoperative complications occurred in 51.0% of patients, with pancreatic fistulae developing in 27.6%. GNRI demonstrated superior predictive accuracy for both 90-day and long-term mortality compared to PNI and TBAR. Lower GNRI scores were significantly associated with worse survival outcomes. Multivariate Analysis revealed that age, GNRI, and the presence of postoperative complications were independent predictors of 90-day mortality. GNRI was the only significant predictor of long-term mortality in the Cox regression model.

Conclusion: Preoperative GNRI demonstrated superior predictive performance compared to PNI and TBAR in predicting postoperative survival following PD in elderly patients. Lower GNRI scores were strongly associated with increased mortality risk. We suggest routine screening for malnutrition using tools like GNRI to identify these vulnerable patients at increased risk of mortality following PD.

Keywords: Elderly, geriatrics, geriatric nutritional risk index, nutrition, pancreaticoduodenectomy, prognostic nutritional index, survival

INTRODUCTION

Pancreaticoduodenectomy (PD) remains a complex gastrointestinal surgery primarily indicated for malignant pancreatic head tumors. Despite advancements in surgical techniques and postoperative care, it is associated with significant morbidity and mortality, with rates as high as 60% and 5%, respectively.[1,2] Patient characteristics, preoperative clinical status, and ability to tolerate the procedure and its complications are key factors influencing outcomes.[3]

Ongoing research aims to reduce these risks by addressing both patient-related and surgical factors.

The pancreas plays a crucial role in both digestion and glycemic control. Unfortunately, up to 80% of pancreatic cancer patients experience nutritional deficiencies due to pancreatic exocrine and endocrine insufficiency.[4] Various scoring systems are employed to assess the nutritional status of these patients. The geriatric nutritional risk index (GNRI) is a widely used index for estimating nutritional status in elderly patients with chronic kidney disease and heart failure.[5] Another common tool is the prognostic nutritional index (PNI), which measures a patient's nutritional and systemic immunological status. PNI is calculated based on serum albumin concentrations and total lymphocyte counts in peripheral blood and is used to assess perioperative immune nutritional status.[6]

Total bilirubin albumin ratio (TBAR) is another important prognostic factor for pancreatic cancer patients. Preoperative total bilirubin, a marker of biliary obstruction, is elevated in most patients with pancreatic tumors at diagnosis. Albumin, reflecting immune and nutritional status, has also been widely used. TBAR, a combination of these two, has been shown to

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predict prognosis in pancreatic cancer.[7] While these indices have been studied for predicting postoperative outcomes in PD patients, their comparative performance in elderly patients remains unexplored. Therefore, the aim of this study was to evaluate the prognostic significance of nutritional indices including GNRI, PNI, and TBAR in predicting postoperative outcomes following PD among elderly patients.

METHODS

Ethics

The study was conducted with the permission of the Clinical Researches Ethics Committee of Adana City Training and Research Hospital (Date: 18.01.2024, Decision No: 3103). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Patients and Data Collection

Patient data was collected from the hospital information management system. A flowchart of the study population is shown in **Figure 1**. Tumor diameter was defined as the maximum diameter of the lesion in the surgical specimen.

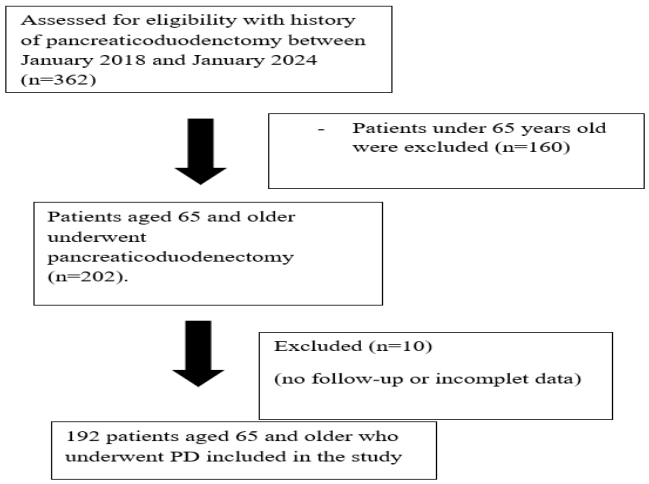
Assessed for eligibility with history of pancreaticoduodenctomy between January 2018 and January 2024 (n=362)
- Patients under 65 years old were excluded (n=160)
Patients aged 65 and older underwent pancreaticoduodenectomy (n=202).
Excluded (n=10)
(no follow-up or incomplet data)
192 patients aged 65 and older who underwent PD included in the study

Figure 1. Flowchart of the study population

Postoperative survival was defined as survival beyond 90 days. All deaths that occurred during the follow-up were included in the assessment of long-term mortality.

All surgeries were performed by a specialized surgical team.

Existing diagnoses in hospital medical records were evaluated, and diagnoses were compiled according to the International Classification of Diseases (ICD) system. Postoperative complications were graded using the Clavien-Dindo classification, a widely used system for categorizing complications based on severity.[8]

The Clavien-Dindo classification ranges from grade I (minor complications requiring pharmacological treatment or minor interventions) to grade V (death), with increasing severity. Grade II includes complications requiring invasive intervention (e.g., drainage, endoscopic procedures). Grade IIIa encompasses serious complications requiring non-operative intervention, while Grade IIIb involves serious complications requiring operative, endoscopic, or radiological intervention. Grade IV represents life-threatening complications.

In addition, the duration of hospital stay, and The American Society of Anesthesiologists (ASA) physical status classification system score of the patients were noted.

GNRI and PNI Calculation

The GNRI was calculated based on serum albumin concentration and body weight.[9-11]

The PNI was calculated using the formula:

PNI=Serum albumin level (g/L)+5×total lymphocyte count (10^9/L).[6]

Unit changes were made as required by the formula.

Serum albumin and total lymphocyte counts were obtained within one week before surgery.

Statistical Analysis

Numerical variables were summarized as mean±standard deviation or median with interquartile range (IQR). Categorical variables were summarized as frequencies and percentages. Normality of distribution was assessed using the Kolmogorov-Smirnov test.

The Chi-square test was used to compare categorical variables between groups. In cases where the expected value was lower, cells were merged and Fisher's exact test was used where necessary. An independent sample t-test was used for normally distributed data. The Mann-Whitney U test was used for non-normally distributed data.

The Kaplan-Meier method was used to estimate survival probabilities. The log-rank test was used to compare survival curves between groups. Cox proportional hazards regression analysis was performed to identify predictors of overall survival. A forward stepwise selection procedure was used to build the final model.

Receiver operating characteristic (ROC) curve analysis was performed to assess the predictive ability of GNRI and PNI for 90-days and overall mortality. Optimal cut-off points were determined using the Youden index. Sensitivity and specificity were calculated to evaluate diagnostic accuracy.

Statistical analyzes were conducted using IBM SPSS Statistics 20.0. A p-value of less than 0.05 was considered statistically significant.

RESULTS

The study included 192 participants (52.6% female, 47.4% male) with a mean age of 71.6±5.3 years (range: 65–87 years).

56.3% of participants had at least one systemic comorbidity, such as diabetes mellitus (19.3%), hypertension (28.6%), or coronary artery disease (19.3%).

The mean follow-up time was 22.5±20.9 months (median: 15.0 months, IQR: 6.0-36.0).

Demographic characteristics, clinical findings, and patient scores are summarized in **Table 1**. Continuous variables are presented as mean±standard deviation or median with IQR. Categorical variables are presented as frequencies and percentages.

Table 1. Demographic characteristics and clinical findings of the pancreaticoduodenectomy patients

Age	71.6±5.3
Median follow-up time (month)	15.0 (6.0-36.0)
Lymphocyte (10^3/μL)	1550 (1200-2200)
PNI (mean±SD)	42.5±7.5
GNRI, median (IQR)	92.0 (82.0-100.0)
Total bilirubin-albumin ratio median (IQR)	0.2 (0.1-1.0)
Total bilirubin (μmol/L) median (IQR)	7.2 (3.3-28.8)
Albumin (g/L) (mean±SD)	33.5±5.2
Duration of hospital stay (day) median (IQR)	12.0 (8.0-19.0)
Tumor diameter (cm) median (IQR)	3.0 (2.0-4.0)
Gender (female/male) n (%)	101 (52.6)/ 91 (47.4)
Long term mortality alive/exitus, n (%)	109 (56.8)/ 83 (43.2)
90 day mortality alive/exitus, n (%)	161 (83.9)/31 (16.1)
ASA score n (%)	
1	1 (0.5)
2	41 (21.4)
3	122 (63.5)
4	28 (14.6)
Systemic disease (+/-) n (%)	108 (56.3)/84 (43.8)
Diabetes mellitus (+/-) n (%)	37 (19.3)/155 (80.7)
Hypertension (+/-) n (%)	55 (28.6)/137 (71.4)
Coroner artery disease (+/-) n (%)	37 (19.3)/155 (80.7)
Systemic complication (+/-) n (%)	98 (51.0)/94 (49.0)
Pancreatic fistula (+/-) n (%)	53 (27.6)/139 (72.4)
GNRI category n (%)	
Low risk	70 (36.5)
Moderate risk	29 (15.1)
High risk	93 (48.4)
Malignant etiology/benign etiology	157 (81.8)/35 (18.2)

PNI: Prognostic nutritional index, SD: Standard deviation, GNRI: Geriatric nutritional risk index, IQR: Interquartile range, ASA: The American Society of Anesthesiologists

Comparison of patients who died within 90 days (exitus group) versus those who survived (alive group) revealed that the exitus group had a significantly higher mean age (p=0.012).

The exitus group exhibited significantly lower mean PNI scores (39.4±8.4 vs. 43.1±7.2, p=0.012) and lower median GNRI (80, IQR: 75-86 vs. 85-101, p<0.001). The exitus group experienced a significantly higher rate of postoperative complications (80.6% vs. 45.1%, p<0.001).

Notably, no significant differences were found between the groups with respect to lymphocyte counts, gender distribution, prevalence of systemic diseases (including diabetes, hypertension, and coronary artery disease), malignancy rates, tumor diameter, or total bilirubin levels (Table 2).

A multivariate logistic regression model was constructed using variables that demonstrated statistical significance in the univariate analysis. Age, GNRI, and the presence of postoperative complications were included as independent variables. PNI was excluded from the model due to its high correlation with GNRI. Albumin was also excluded as it is a component of both PNI and GNRI and exhibited strong correlations with these variables. Pancreatic fistulae were observed in only three patients in the mortality group, precluding their inclusion in the multivariate model.

The model revealed the following significant predictors of 90-day mortality:

Increasing age was associated with a 1.08-fold increase in the odds of mortality (OR: 1.08, 95% CI: 1.01-1.17). A decrease in GNRI was associated with a 1.1-fold increase in the odds of mortality (OR: 0.89, 95% CI: 0.86-0.94). The presence of postoperative complications was associated with a 6-fold increase in the odds of mortality (OR: 6.0, 95% CI: 2.1-17.2).

Receiver Operating Characteristic (ROC) Curve Analysis

The AUC for PNI was 0.635 (p=0.017, 95% CI: 0.523-0.747), indicating moderate accuracy in predicting 90-day mortality. The optimal cut-off point for PNI was determined to be <36.65, yielding a sensitivity of 45.2% and a specificity of 80.1%.

The AUC for GNRI was significantly higher at 0.799 (p<0.001, 95% CI: 0.725-0.872), suggesting strong discriminatory ability. The optimal cut-off point for GNRI, determined using the Youden index, was <91.5, achieving a sensitivity of 93.5% and a specificity of 60.2%.

The AUC for TBAR was 0.438 (p=0.272, 95% CI: 0.348-0.527), which was not statistically significant (Figure 2).

Long-Term Mortality Analysis

Table 3 presents the results of the analysis of factors associated with long-term mortality. The exitus group exhibited a significantly higher mean age (p=0.018).

The exitus group had significantly lower lymphocyte levels (p=0.027).

Mean PNI scores were significantly lower in the exitus group (p=0.001).

Median GNRI scores were significantly lower in the exitus group [81 (IQR: 77-88)] compared to the alive group [99 (IQR: 94-103)] (p<0.001).

The exitus group had significantly higher levels of TBAR (p=0.029).

Statistical Analysis

The analysis revealed a significant difference in survival rates across Clavien-Dindo classification grades (χ^2=50.837, p<0.001). The exitus group demonstrated a significantly higher malignancy rate (90.4% vs. 75.2%, p=0.008). 59.6% of the Alive group was classified as low-risk according to GNRI, while 85.5% of the exitus group was classified as high-risk (p<0.001). No significant differences were observed between the groups regarding gender, systemic diseases (including diabetes, hypertension, and coronary artery disease), complications, or pancreatic fistula (Table 3).

Receiver Operating Characteristic (ROC) Curve Analysis

ROC curve analysis demonstrated an AUC of 0.649 (95% CI: 0.570-0.728) for PNI, indicating moderate accuracy in

Table 2. Risk factors affecting 90-day in pancreaticoduodenectomy patients

	Alive	Ex	p value
Age (years)	71.1±5.0	73.7±6.1	0.012
Lymphocyte (10^3/μL)	1600 (1200-2200)	1500 (1000-2300)	0.588
PNI (mean±SD)	43.1±7.2	39.4±8.4	0.012
GNRI (mean±SD)	94 (85-101)	80 (75-86)	<0.001
Total bilirubin-albumin ratio (TBAR)	0.2 (0.1-1)	0.3 (0.2-0.9)	0.272
Total bilirubin (μmol/L)	7.2 (3.3-28.9)	7.2 (5-21.1)	0.512
Albumin (g/L)	34.1±5.0	30.5±5.4	<0.001
Duration of hospital of stay (day)	12 (9-18)	11 (4-23)	0.233
Tumor diameter (cm)	2.8 (2-4)	3.5 (2.5-4)	0.079
Gender (F/M) n (%)	84 (52.2)/77 (47.8)	17 (54.8)/14 (45.2)	0.846
ASA			
1+2	36 (22.4)	6 (19.3)	0.816
3+4	125 (77.3)	25 (80.6)	
Systemic disease (+/-) n (%)	90 (55.9)/71 (44.1)	18 (58.1)/13 (41.9)	0.846
DM (+/-) n (%)	33 (20.5)/128 (79.5)	4 (12.9)/27 (87.1)	0.457
HT (+/-) n (%)	46 (28.6)/115 (71.4)	9 (29)/22 (71)	0.959
CAD (+/-) n (%)	30 (18.6)/131 (81.4)	7 (22.6)/24 (77.4)	0.622
Complication (+/-) n (%)	73 (45.3)/88 (54.7)	25 (80.6)/6 (19.4)	<0.001
Pancreatic fistula (+/-) n (%)	50 (31.1)/111 (68.9)	3 (9.7)/28 (90.3)	0.015
Etiology n (%) Malignant Benign	 130 (80.7) 31 (19.3)	 27 (87.1) 4 (12.9)	0.611

PNI: Prognostic nutritional index, SD: Standard deviation, GNRI: Geriatric nutritional risk index, ASA: The American Society of Anesthesiologists, DM: Diabetes mellitus, HT: Hypertension, CAD: Coronary artery disease

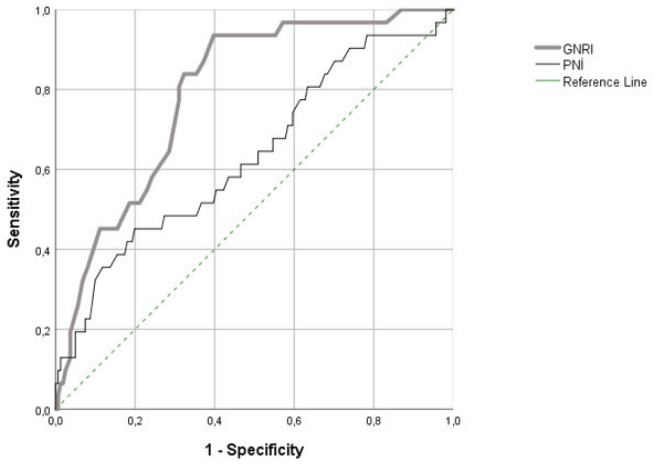

Figure 2. ROC curve of PNI and GNRI for 90-day in PD

ROC: Receiver operating characteristic, PNI: Prognostic nutritional index, GNRI: Geriatric nutritional risk index, PD: Pancreaticoduodenectomy patients

predicting long-term mortality (p<0.001). The optimal cut-off point for PNI, determined using the Youden index, was <42.55, with a sensitivity of 65.1% and a specificity of 62.4%.

In contrast, GNRI exhibited a significantly higher AUC of 0.890 (95% CI: 0.842-0.938), suggesting strong discriminatory ability in predicting long-term mortality (p<0.001). The optimal cut-off point for GNRI was <92.5, with a sensitivity of 91.6% and a specificity of 78.9% (**Figure 3**).

Cox Regression Analysis

Cox regression analysis was performed to assess the impact of prognostic factors on survival. Variables included in the analysis were age, PNI, GNRI-score, tumor diameter, and etiology, all of which demonstrated significance in univariate Cox regression.

The final Cox regression model was constructed using the Forward LR method, incorporating only statistically significant variables.

The results revealed that only the GNRI significantly affected mortality. Decreased GNRI score was found to be a risk factor for mortality (HR:1.09, 95%ci: 1.07-1.12).

DISCUSSION

The world's elderly population is rapidly expanding. While surgical techniques and medical cancer treatments for older adults have advanced significantly, deciding on surgery for this group remains challenging. PD is a potentially curative surgical option widely used in pancreatic cancer treatment. However, its safety in the elderly is debated due to higher observed mortality and morbidity rates in this population. Researchers have highlighted that geriatric assessment can help identify elderly patients at high risk for complications from PD.[12] In our study, preoperative GNRI demonstrated superior predictive performance compared to PNI and TBAR in predicting postoperative survival following PD in elderly patients. Lower GNRI scores were strongly associated with increased mortality risk.

Ito et al.[13] reported that there was no significant difference between the two groups in terms of PD results in their study comparing patients over 75 years of age and younger group.

Table 3. Risk factors affecting long-term mortality mortality in the pancreaticoduodenectomy patients

	Mortality		
	Alive	**Ex**	**p value**
Age (years)	70.7±4.5	72.6±6.1	0.018
Lymphocyte (10^3/μL)	1700 (1300-2300)	1400 (1000-2200)	0.027
PNI (mean±SD)	44.1±7.1	40.4±7.7	0.001
GNRI median (IQR)	99 (94-103)	81 (77-88)	<0.001
Total bilirubin-albumin ratio (TBAR)	0.2 (0.1-0.8)	0.3 (0.1-1)	0.029
Total bilirubin (μmol/L) median (IQR)	5.6 (2.8-26.1)	11.7 (4.4-29.4)	0.057
Albumin (g/L) (mean±SD)	34.7±5.2	31.9±4.8	<0.001
Duration of hospital of stay (day) median (IQR)	12 (9-17)	12 (8-19)	0.892
Tumor diameter (cm) median (IQR)	2.5 (1.7-4)	3 (2.1-4)	0.025
Clavien-Dindo classification n (%)			
0	2 (1.8)	0 (0.0)	<0.001
1	14 (12.8)	1 (1.2)	
2	49 (45.0)	30 (36.1)	
3	34 (31.2)	18 (21.7)	
4	10 (9.2)	5 (6.0)	
5	0 (0.0)	29 (34.9)	
Gender (female/male) n (%)	56 (51.4)/53 (48.6)	45 (54.2)/38 (45.8)	0.696
ASA n (%)			
1+2	28 (25.7)	14 (16.9)	0.161
3+4	81 (74.3)	69 (83.1)	
Systemic disease (+/-)	60 (55.0)/49 (45.0)	48 (57.8)/35 (42.2)	0.700
DM	24 (22.0)/85 (78.0)	13 (15.7)/70 (84.3)	0.269
HT	31 (28.4)/78 (71.6)	24 (28.9)/59 (71.1)	0.942
CAD	20 (18.3)/89 (81.7)	17 (20.5)/66 (79.5)	0.710
Complication (+/-) n (%)	54 (49.5)/55 (50.5)	44 (53)/39 (47)	0.634
Etiology n(%)			
Malignant	82 (75.2)	75 (90.4)	0.008
Benign	27 (24.8)	8 (9.6)	

PNI: Prognostic nutritional index, SD: Standard deviation, GNRI: Geriatric nutritional risk index, IQR: Interquartile range, ASA: The American Society of Anesthesiologists, DM: Diabetes mellitus, HT: Hypertension, CAD: Coronary artery disease

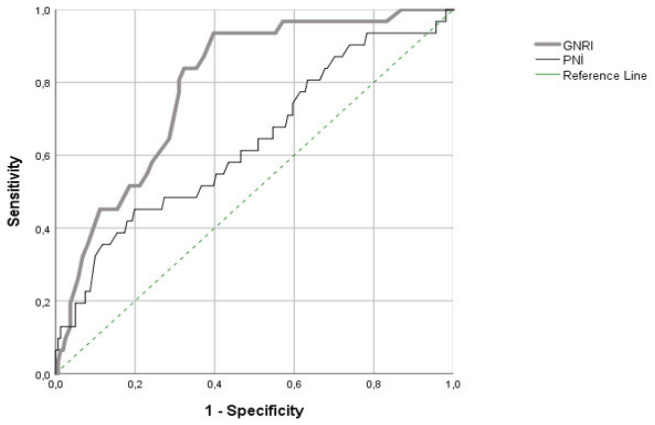

Figure 3. ROC curve of PNI and GNRI for long term mortality

ROC: Receiver operating characteristic, PNI: Prognostic nutritional index, GNRI: Geriatric nutritional risk index

A different study reported that age-related care should be designed to reduce the impact of complications in elderly patients, including geriatric consultation, supplemental enteral nutrition and early rehabilitation placement planning.[14]

Flores et al.[15] observed higher postoperative mortality and nonsurgical complications in elderly patients. While their study did not find a direct correlation between age and survival, it emphasized the importance of considering patient selection to mitigate complication risks.

In contrast, our study focused on comparing patients aged above 65 years based on 90-day survival outcomes. We observed a statistically significant difference in mean age, with the surviving group demonstrating a lower mean age compared to the non-surviving group (73.7 years). Furthermore, the group with a shorter survival time (less than 90 days) exhibited a statistically significant increase in complications, with pancreatic fistula identified as the most prevalent complication.

The elderly are at risk of physical, psychological and/or physiological dysfunctions and associated malnutrition as a result of a cascade of events triggered by cellular aging.[7] In addition, the impact of malnutrition extends beyond its physiological consequences. Contributes to an increased risk of a decline in quality of life, performance status and

resistance to infections due to reduced immune function.[16] However, nutritional disorders due to hormonal and enzymatic effects in pancreatic tumors make elderly patients particularly vulnerable to malnutrition.[4,17,18] Therefore, it is recommended to determine the nutritional status of elderly patients before PD. Kim et al.[19] investigated the effects of preoperative nutritional status on PD outcomes and reported that preoperative malnourished patients suffered from poor clinical outcomes, therefore, necessary intervention should be performed before surgery in patients with malnutrition.

A study conducted in Japan reported that preoperative nutritional status was effective in predicting complications after PD. Therefore, the use of scales indicating nutritional status before PD was recommended.[20] A study by Kanda et al.[21] on pancreatic cancer patients found that a low preoperative PNI score was associated with more postoperative complications, including pancreatic fistula, but was insufficient to predict long-term survival.

In a study on patients undergoing various surgical interventions, Gibbs et al.[22] showed that the 30-day postoperative mortality rate increased from 1% in patients with albumin levels >4.6 mg/dl to 28% in patients with albumin levels <2.1 mg/dl, indicating a positive relationship between preoperative low albumin levels and mortality. Several other studies have also used hypoalbuminemia as a component of perioperative predictive scoring models assessing frailty and fitness to predict pancreatic cancer and pancreatic surgery outcomes.[23,24] While the ASA score is a widely utilized tool for pre-operative risk assessment, our analysis revealed no statistically significant difference in ASA scores between patients who survived and those who died following Whipple surgery. This suggests that the ASA score, which primarily reflects pre-existing comorbidities and is subject to inter-observer variability, it may not be able to accurately show the physiological stress of the surgery itself or the development of post-operative complications, which are major determinants of mortality after a Whipple surgery. Specifically, post-operative complications and pancreatic fistulas emerged as significant predictors of 90-day mortality, indicating that post-operative events likely play a critical role in patient outcomes.

Low albumin values cause low GNRI and PNI results.[10,11] Our study showed that preoperative nutritional status, as assessed by albumin levels, PNI, and GNRI, significantly impacts 90-day survival in geriatric patients undergoing PD. Patients with higher albumin levels and lower PNI/GNRI scores had significantly higher mortality rates.

ROC curve analysis revealed that GNRI exhibited strong predictive ability for 90-day mortality compared to PNI. Multivariate analysis confirmed GNRI as an independent predictor of mortality. Unlike GNRI, the PNI calculation takes into account the number of lymphocytes in addition to albumin, which is also suggestive of immunity.[10,11] Therefore, PNI was preferred more in determining the preoperative nutritional status in our center previously. However, our results have shown that preoperative GNRI values are more successful in predicting postoperative PD survival. Therefore, we think that it is important to consider preoperative GNRI results.

Unlike the GNRI, PNI calculation considers both albumin levels and lymphocyte counts, which reflect immune function.[10,11] This broader assessment makes PNI more commonly used for evaluating preoperative nutritional status at our institution. However, our findings indicate that preoperative GNRI values are more effective in predicting postoperative mortality. Therefore, we believe that preoperative GNRI assessment remains crucial.

Limitations

The most important limitation of this study is that it is retrospective, and the sample size is limited. Excluding patients younger than 65 years was the potential selection bias for this study because it may limit the generalizability of the findings to the broader population of PD patients.

CONCLUSION

Preoperative GNRI demonstrated superior predictive performance compared to PNI and TBAR in predicting postoperative survival following PD in elderly patients.

Lower GNRI scores were strongly associated with increased mortality risk. We suggest routine screening for malnutrition using tools like GNRI to identify these vulnerable patients at increased risk of mortality following PD.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was conducted with the permission of the Clinical Researches Ethics Committee of Adana City Training and Research Hospital (Date: 18.01.2024, Decision No: 3103).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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